Complete Summary

GUIDELINE TITLE

Clinical policy: critical issues in the management of patients presenting to the emergency department with acetaminophen overdose.

BIBLIOGRAPHIC SOURCE(S)

Wolf SJ, Heard K, Sloan EP, Jagoda AS, American College of Emergency Physicians. Clinical policy: critical issues in the management of patients presenting to the emergency department with acetaminophen overdose. Ann Emerg Med 2007 Sep;50(3):292-313. [55 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Acetaminophen overdose

GUIDELINE CATEGORY

Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Emergency Medicine
Gastroenterology
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To address the following two critical questions:

- What are the indications for *N*-acetylcysteine (NAC) in the acetaminophen overdose patient with a known time of acute ingestion who can be risk stratified by the Rumack-Matthew nomogram?
- What are the indications for NAC in the acetaminophen overdose patient who cannot be risk stratified by the Rumack-Matthew nomogram?

TARGET POPULATION

Patients older than 12 years presenting to the emergency department (ED) with acetaminophen overdose

These guidelines are *not* intended for patients 12 years or younger.

INTERVENTIONS AND PRACTICES CONSIDERED

1. Use of *N*-acetylcysteine (NAC) in the acetaminophen overdose patient with a known time of acute ingestion who can be risk stratified by the Rumack-Matthew nomogram
2. Use of NAC in the acetaminophen overdose patient who cannot be risk stratified by the Rumack-Matthew nomogram

MAJOR OUTCOMES CONSIDERED

- Hepatotoxicity
- Hepatic failure
- Disease progression in the setting of hepatic failure believed to be due to acetaminophen toxicity
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE searches for articles published between January 1974 and January 2006 were performed using a combination of key words and their variations, including "acetaminophen," "paracetamol," "APAP," "extended release," "acetylcysteine," "*N*-acetylcysteine," "Mucomyst," "NAC," "liver disease," "aminotransferase," "aspartate transaminase," "alanine transferase," "SGOT," "AST," "ALT," and "hepatitis, toxic." Searches were limited to English-language sources. Additional articles were reviewed from the bibliography of articles cited and from published textbooks and review articles. Subcommittee members also supplied articles from their own files.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Strength of Evidence

Literature Classification Schema^

Design/Class	Therapy*	Diagnosis**	Prognosis***
1	Randomized, controlled trial or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)	Case series Case report Other (e.g., consensus, review)

^Some designs (e.g., surveys) will not fit this schema and should be assessed individually.

*Objective is to measure therapeutic efficacy comparing ≥2 interventions.

**Objective is to determine the sensitivity and specificity of diagnostic tests.

***Objective is to predict outcome including mortality and morbidity.

Approach to Downgrading Strength of Evidence

Downgrading	Design/Class		
	1	2	3

Downgrading	Design/Class		
	1	2	3
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

This clinical policy was created after careful review and critical analysis of the medical literature.

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members for strength of evidence and classified by the subcommittee members into 3 classes of evidence on the basis of the design of the study, with design 1 representing the strongest evidence and design 3 representing the weakest evidence for therapeutic, diagnostic, and prognostic clinical reports, respectively (see Appendix A in the original guideline document and the "Rating Scheme for the Strength of the Evidence" field). Articles were then graded on 6 dimensions thought to be most relevant to the development of a clinical guideline: blinded versus nonblinded outcome assessment, blinded or randomized allocation, direct or indirect outcome measures (reliability and validity), biases (e.g., selection, detection, transfer), external validity (i.e., generalizability), and sufficient sample size. Articles received a final grade (Class I, II, III) on the basis of a predetermined formula, taking into account design and quality of study (see Appendix B in the original guideline document and the "Rating Scheme for the Strength of the Evidence" field). Articles with fatal flaws were given an "X" grade and not used in formulating recommendations in this policy. Evidence grading was done with respect to the specific data being extracted and the specific critical question being reviewed. Thus, the level of evidence for any one study may vary according to the question, and it is possible for a single article to receive different levels of grading as different critical questions are answered. Question-specific level of evidence grading may be found in the Evidentiary Table included at the end of the original guideline document.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This policy is a product of the American College of Emergency Physicians (ACEP) clinical policy development process, including expert review, and is based on the existing literature; where literature was not available, consensus of emergency physicians was used.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Clinical findings and strength of recommendations regarding patient management were made according to the following criteria:

Strength of Recommendations

Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (i.e., based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues)

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (i.e., based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies)

Level C recommendations. Other strategies for patient management that are based on preliminary, inconclusive, or conflicting evidence, or, in the absence of any published literature, based on panel consensus

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, strength of prior beliefs, and publication bias, among others, might lead to such a downgrading of recommendations.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Expert review comments were received from individual emergency physicians and toxicologists and individual members from the American Academy of Pediatrics Committee and Section on Pediatric Emergency Medicine, American Association for the Study of Liver Diseases, American Gastroenterological Association, and the American College of Emergency Physicians' (ACEP's) Toxicology Section. Their responses were used to further refine and enhance this policy.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the strength of evidence (Class I-III) and strength of recommendations (Level A-C) are repeated at the end of the Major Recommendations.

1. **What are the indications for *N*-acetylcysteine (NAC) in the acetaminophen overdose patient with a known time of acute ingestion who can be risk stratified by the Rumack-Matthew nomogram?**

   Level A recommendations. None specified.

   Level B recommendations.

   1. Administer NAC to acute acetaminophen overdose patients with either *possible* or *probable* risk for hepatotoxicity as determined by the Rumack-Matthew nomogram to reduce the incidence of severe hepatotoxicity and mortality, ideally within 8 to 10 hours postingestion.
   2. Do not administer NAC to acute acetaminophen overdose patients with *no* risk for hepatotoxicity as determined by the Rumack-Matthew nomogram.

   Level C recommendations. None specified.

2. **What are the indications for NAC in the acetaminophen overdose patient who cannot be risk stratified by the Rumack-Matthew nomogram?**

   Level A recommendations. None specified.

   Level B recommendations. Administer NAC to patients with hepatic failure thought to be due to acetaminophen.

   Level C recommendations. Administer NAC to patients who have hepatotoxicity thought to be due to acetaminophen and have a suspected or known acetaminophen overdose, including repeated supratherapeutic ingestions.

Definitions:

Literature Classification Schema^

Design/Class	Therapy*	Diagnosis**	Prognosis***
1	Randomized, controlled trial or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series	Case series	Case series

Design/Class	Therapy*	Diagnosis**	Prognosis***
	Case report Other (e.g., consensus, review)	Case report Other (e.g., consensus, review)	Case report Other (e.g., consensus, review)

^Some designs (e.g., surveys) will not fit this schema and should be assessed individually.

*Objective is to measure therapeutic efficacy comparing ≥2 interventions.

**Objective is to determine the sensitivity and specificity of diagnostic tests.

***Objective is to predict outcome including mortality and morbidity.

Approach to Downgrading Strength of Evidence

Downgrading	Design/Class		
	1	2	3
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

*See "Description of Methods Used to Analyze the Evidence" field for more information.

Strength of Recommendations

Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (i.e., based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues)

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (i.e., based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies)

Level C recommendations. Other strategies for patient management that are based on preliminary, inconclusive, or conflicting evidence, or, in the absence of any published literature, based on panel consensus

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, strength of prior beliefs, and publication bias, among others, might lead to such a downgrading of recommendations.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate evaluation, risk assessment, and management of patients presenting to the Emergency Department (ED) with acetaminophen overdose

POTENTIAL HARMS

- *N*-acetylcysteine (NAC) given orally has been shown to have a minimal adverse effect profile, consisting mostly of nausea and emesis, and increased tolerance can be achieved with co-administration of an antiemetic.
- Common adverse effects of intravenous NAC include pruritus, flushing, and a rash (approximately 15% of patients), which is most often treated by holding the infusion, administering an antihistamine, and restarting the infusion at a lower rate. Bronchospasm and hypotension are rare. Fatal reactions are rare but have been reported.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Recommendations offered in this policy are not intended to represent the only diagnostic and management options that the emergency physician should consider. The American College of Emergency Physicians (ACEP) clearly recognizes the importance of the individual physician's judgment. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the crucial questions addressed in this policy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Wolf SJ, Heard K, Sloan EP, Jagoda AS, American College of Emergency Physicians. Clinical policy: critical issues in the management of patients presenting to the emergency department with acetaminophen overdose. Ann Emerg Med 2007 Sep;50(3):292-313. [55 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Jun

GUIDELINE DEVELOPER(S)

American College of Emergency Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Emergency Physicians

GUIDELINE COMMITTEE

American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Critical Issues in the Management of Patients Presenting to the Emergency Department With Acetaminophen Overdose

American College of Emergency Physicians Clinical Policies Committee (Oversight Committee)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Subcommittee (Writing Committee) on Critical Issues in the Management of Patients Presenting to the Emergency Department With Acetaminophen Overdose:

Stephen J. Wolf, MD (Chair); Kennon Heard, MD; Edward P. Sloan, MD, MPH; Andy S. Jagoda, MD

American College of Emergency Physicians Clinical Policies Committee (Oversight Committee): Andy S. Jagoda, MD (Chair 2003-2006, Co-Chair 2006-2007); Wyatt W. Decker, MD (Co-Chair 2006-2007); Deborah B. Diercks, MD; Jonathan A. Edlow, MD; Francis M. Fesmire, MD; Steven A. Godwin, MD; Sigrid A. Hahn, MD; John M. Howell, MD; J. Stephen Huff, MD; Thomas W. Lukens, MD, PhD; Donna L. Mason, RN, MS, CEN (ENA Representative 2004-2006); Michael Moon, RN, CNS, MSN, CEN (ENA Representative 2004); Anthony M. Napoli, MD (EMRA Representative 2004-2006); Devorah Nazarian, MD; Jim Richmann, RN, BS, MA(c), CEN (ENA Representative 2006-2007); Scott M. Silvers, MD; Edward P. Sloan, MD, MPH; Molly E. W. Thiessen, MD (EMRA Representative 2006-2007); Robert L. Wears, MD, MS (Methodologist); Stephen J. Wolf, MD; Cherri D. Hobgood, MD (Board Liaison 2004-2006); David C. Seaberg, MD, CPE (Board Liaison 2006-2007); Rhonda R. Whitson, RHIA, Staff Liaison, Clinical Policies Committee and Subcommittees

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Relevant industry relationships for the following Acetaminophen Overdose Subcommittee members are as follows: Dr. Heard is the Medical Toxicology Fellowship Director at the Rocky Mountain Poison and Drug Center, which has research and business contracts with McNeil Consumer Products and Cumberland Pharmaceuticals. Dr. Heard has received honoraria from Cumberland Pharmaceuticals and from McNeil Consumer Products to provide educational lectures and materials for projects other than this clinical policy.

Relevant industry relationships are those relationships with companies associated with products or services that significantly impact the specific aspect of disease addressed in the critical question.

ENDORSER(S)

Emergency Nurses Association - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Emergency Physicians Web site.

Print copies: Available from the American College of Emergency Physicians, P.O. Box 619911, Dallas, TX 75261-9911, or call toll free: (800) 798-1822.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on January 21, 2008. The information was verified by the guideline developer on February 15, 2008.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 9/22/2008


DEPARTMENT OF HEALTH & HUMAN SERVICES • USA